

Application No. 09/498,046  
Response Dated April 13, 2005 to  
January 13, 2005 Office Action

**Amendments to the Claims:**

Claim 34 is amended as indicated below. The following listing of claims will replace all prior versions and listings of claims in the application.

**Listing of Claims:**

1-25. (Cancelled)

26. (Previously Presented) A human influenza vaccine comprising a fusion product, said fusion product comprising

(i) an immunogenic extracellular part of (a) an M2 membrane protein of a human influenza A virus, (b) an NB protein of a human influenza B virus, or (c) a CM2 protein of a human influenza C virus, and

(ii) a heterologous presenting carrier.

27. (Previously Presented) The influenza vaccine of claim 26, wherein the presenting carrier is a peptide or polypeptide.

28. (Previously Presented) The influenza vaccine of claim 27, wherein the presenting peptide or polypeptide is selected from the group consisting of a hepatitis B core protein, C3d, polypeptides comprising multiple copies of C3d, tetanus toxin fragment C and yeast Ty particles.

29. (Previously Presented) The influenza vaccine of claim 26, wherein the presenting carrier is a non-peptidic structure.

30. (Previously Presented) The influenza vaccine of claim 29, wherein the presenting non-peptidic structure is selected from the group consisting of glycans, polyethylene glycols, peptide mimetics, and synthetic polymers.

31. (Previously Presented) The influenza vaccine of claim 26, wherein the presenting carrier enhances the immunogenicity of the antigen.

32. (Previously Presented) The influenza vaccine of claim 31, wherein the presenting carrier comprises an epitope recognized by an influenza-specific T helper cell or cytotoxic T cell.

33. (Cancelled)

34. (Currently Amended) The influenza vaccine of claim 26, wherein the vaccine antigen comprises Lactococci cells expressing said fusion product in or on their cell membrane, and said cells optionally release said fusion product.

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35. (Cancelled)

36. (Previously Presented) The influenza vaccine of claim 26, wherein the fusion product is in an isolated form.

37. (Previously Presented) The influenza vaccine of claim 26, wherein the fusion product is anchored in the membrane of an acceptor cell expressing the fusion product.

38. (Previously Presented) The influenza vaccine of claim 26, wherein the fusion product is part of a lipid bilayer or cell wall.

39. (Previously Presented) The influenza vaccine of claim 26, wherein the influenza vaccine comprises Lactococci cells expressing the fusion product in or on their cell wall.

40. (Previously Presented) The influenza vaccine of claim 26, further comprising an influenza antigen selected from the group consisting of hemagglutinin, neuraminidase, nucleoprotein and native M2.

41. (Previously Presented) A method of obtaining a human influenza vaccine, comprising

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providing a fusion product, said fusion product comprising (i) an immunogenic extracellular part of (a) an M2 membrane protein of a human influenza A virus, (b) an NB protein of a human influenza B virus, or (c) a CM2 protein of a human influenza C virus, and (ii) a heterologous presenting carrier; and

mixing it with an excipient.

42. (Withdrawn) A nucleic acid construct encoding a fusion product, said fusion product comprising

(i) an extracellular part of an influenza M2 membrane protein or a functional fragment thereof or modified versions thereof, and

(ii) a presenting carrier,

wherein said extracellular part contains all or part of the 23 amino acid extracellular domain (amino acid residues 2 to 24 as shown in Table 1) of an M2 protein of influenza A virus or of a similar integral membrane protein of influenza B or C virus, and

wherein said functional fragment is a fragment of an M2 protein capable of eliciting a statistically significant higher immunoprotection when administered in an immunoprotective dose to test members of a species, as compared to test members of said species not receiving the functional fragment, and

wherein said modified versions comprise one to three amino acid changes but still react with a polyclonal antiserum derived from immunized animals.

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43. (Withdrawn) The nucleic acid construct of claim 42, wherein the presenting carrier is a (poly)peptide.

44. (Withdrawn) A method of obtaining an influenza antigen, comprising:  
providing the nucleic acid construct of claim 42;  
introducing the nucleic acid construct into an acceptor cell;  
culturing the acceptor cell under conditions that allow expression of the fusion product; and

optionally isolating the fusion product from the acceptor cell or its culture medium, thereby obtaining an influenza antigen comprising the fusion product.

45. (Withdrawn) The method of claim 44, wherein the acceptor cell is a *Lactococcus* cell.

46. (Previously Presented) A human influenza vaccine obtained by the following steps:  
providing a nucleic acid construct that encodes a fusion product, said fusion product comprising (i) an immunogenic extracellular part of (a) an M2 membrane protein of a human influenza A virus, (b) an NB protein of a human influenza B virus, or (c) a CM2 protein of a human influenza C virus, and (ii) a heterologous presenting peptide;  
introducing the nucleic acid construct into an acceptor cell;

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culturing the acceptor cell under conditions that allow expression of the fusion product;  
optionally isolating the fusion product from the acceptor cell or its culture medium;  
and  
optionally admixing the fusion product with an excipient,  
thereby obtaining a human influenza vaccine comprising the fusion product.

47. (Withdrawn) An acceptor cell containing the nucleic acid construct of claim 42.

48. (Withdrawn) The acceptor cell of claim 47, wherein the acceptor cell is a Lactococcus cell.

49. (Withdrawn) A method of obtaining a DNA-based or vaccinia-based influenza vaccine, comprising:

providing the nucleic acid construct of claim 42;  
introducing the nucleic acid construct into a host cell; and  
culturing the host cell under conditions that allow replication of the nucleic acid construct, thereby obtaining a DNA-based or vaccinia-based influenza vaccine comprising the nucleic acid construct.

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50. (Withdrawn) A DNA-based influenza vaccine comprising the nucleic acid construct of claim 42.

51. (Withdrawn) A vaccinia-based influenza vaccine comprising the nucleic acid construct of claim 42.

52. (Previously Presented) The influenza vaccine of claim 26, wherein the influenza vaccine comprises a cytokine.

53. (Previously Presented) The influenza vaccine of claim 26, wherein the influenza vaccine comprises a vaccine adjuvant that is not Freund's adjuvant.

54. (Previously Presented) An influenza vaccine for an animal species comprising a fusion product, said fusion product comprising

- (i) an immunogenic extracellular part of (a) an M2 membrane protein of an influenza A virus or (b) an NB protein of an influenza B virus of said animal species; and
- (ii) a heterologous presenting carrier.

55. (Previously Presented) The influenza vaccine of claim 26, wherein the fusion product comprises the entire extracellular domain of the M2 protein.

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56. (Previously Presented) The influenza vaccine of claim 55, wherein the amino acid sequence of said entire extracellular domain is SEQ ID NO:1, 2, or 3.

57. (Previously Presented) The influenza vaccine of claim 26, wherein the fusion product comprises the entire extracellular domain of the NB or CM2 protein.